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10/529,721	03/30/2005	Toshiaki Takeda	506.44955X00	8995

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EXAMINER
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ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,721	TAKEDA ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *7-9* is/are allowed.

6)☐ Claim(s) *1-3 and 10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of an amendment/remarks on 05/30//2007.

2. By the amendment, claims 10-17 have been newly added; claims 1-3 and 7-9 have been amended; and claims 4-6 have been cancelled.

3. Applicant's amendment presenting method of manufacturing (by canceling "use claims" which were rejected under 101 and 112, 2nd paragraph) necessitates a new ground of the rejection in this Office Action.

4. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the term "treating decubitus", does not reasonably provide enablement for the term "preventing" or "preventive". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The American Heritage Dictionary (Second College Edition, 1982) defines the term d "prevent" as "anticipate or counter in advance, to keep from happening". The interpretation of the instant claims allows for the complete cure and eradication or total elimination of decubitis by the administration of said compounds.

There are no known compounds of similar structure which have been demonstrated to prevent or cure decubitus. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "magic bullet" is contrary to our present understanding of pharmacology. One skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" or completely cure or eradication effect.

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the preventive utility of the instant compounds.

The specification provides the effects of reducing in necrosis or wound of epidermis in rabbit model study (Examples 1-2). However, there is no demonstrated correlation that the tests and results apply to the claimed preventive utility embraced by the instant claims.

Since the efficacy of the claimed composition in preventing decubitus mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3 and 10-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. (EP 1 304 323 A1).

Claims read on a composition comprising an N-acylated derivative of hydroxyproline or a salt thereof (claims 1-3 and 13-15); method of using said composition for the prevention decubitus (claims 16-18); and method of manufacturing said composition (claims 10-12). Further limitations include "the N-acylated derivative of hydroxyproline or a salt thereof is contained in an amount of 0.1 to 15% by weight to the total weight" (claims 2, 11, 14 and 17); "an acyl group

of the N-acylated derivative of hydroxyproline is the acyl group having 1 to 24 carbon atoms" (claims 3, 12, 15 and 18).

Kobayashi teaches a composition comprising N-acyl derivative of hydroxyproline or salts thereof, such as an acyl group having 1 to 24 carbon atoms, that is useful for improving skin barrier function or improving atopic dermatitis, wherein said N-acyl derivative of hydroxyproline is contained in an amount of 0.01 to 20% by weight based on the total weight (see para. [0009], [0016]-[0027]) and a method of preparing said composition by mixing the N-acyl derivative of hydroxyproline with pharmaceutically acceptable excipients or carriers (see para. [0031]-[0053] and Example). Kobayashi also teaches that the N-acyl derivatives of hydroxyproline used in the present can be produced by a known method, such as "either by converting a straight or branched, saturated or unsaturated fatty acid having 1 to 24 carbon atoms into a halide such as chloride or a bromide with a halogenating agent such as thionyl chloride or phosgene, and then condensing the halide with the above hydroxyproline; or by converting a fatty acid into an acid anhydride and then reacting the acid anhydride with hydroxyproline" (see para. [0018], [0020]-[0024]).

With respect to the intended use of claims 1-3 and 10-14,

Although Kobayashi is silent about the functional characteristic or property or intended use of said composition in "a preventive or therapeutic agent for decubitis", such characteristic or property deems to be inherent to the referenced composition, i.e., it was always there. Claims to a composition possessing a particular property or characteristics are still properly rejected by a reference to the same composition, even if the referenced does not address or acknowledge the property. Thus, the reference anticipates the claimed invention.

With respect to the preventive utility of method claims 16-18,

The interpretation of the instant claims allow for the inclusion of prophylactic or preventive utility of said composition.

The prior art directing administration of the same composition or compound, in overlapping dosage amounts, inherently possessing same protective utility effect anticipates claims directed to such protective uses encompassed by the instant invention.. Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of compositions.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3 and 13-18 are rejected under the judicially created doctrine of double patenting over claims 1-8 and 15-19 of USP 7138386.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

With respect to the obviousness over the referenced claims 1-6,

Both of the instant application and the patent are directed to the same composition comprising N-acylated hydroxyproline derivative.

Although the patent is silent about the functional characteristic of said N-acylated hydroxproline as "a preventive or therapeutic agent for decubitus", such property or characteristic deems to be inherent to the referenced composition, i.e., it was always there. Claims to a composition possessing a particular property or characteristics are still properly rejected by a reference to the same composition, even if the referenced does not address or acknowledge the property. Thus, the USP'386 makes obvious the instant invention.

With respect to the obviousness over the referenced claims 7-8 and 15-19,

The prior art directing administration of the same composition or compound, in overlapping dosage amounts, inherently possessing same protective utility effect anticipates claims directed to such protective uses encompassed by the instant invention. Thus, the USP'386 makes obvious the instant invention.

Since the interpretation of the instant claims reciting "comprising" allows for the inclusion of any other unspecified ingredients even in major amounts in said composition, the USP'386 makes obvious the instant invention.

With respect to the determination of dosage amounts of said n-acylated derivative in said composition, those of ordinary skill in the art would have been readily optimized effective dosages as determined by good medical practice and the clinical condition of the individual patient. Determination of the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information provided in the prior art.

8. Claims 16-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-20 of copending Application No. 10/250372. Although the conflicting claims are not identical, they are not patentably distinct from each other because the prior art directing administration of the same composition or compound, in overlapping dosage amounts, inherently possessing same protective utility effect anticipates claims directed to such protective uses encompassed by the instant invention. .

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. In looking in continuity data, it is noted that applicant has numerous issued patent and pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, the copending 10/532721, USP 6692754 and USP 6497889 have same or similar subject matter(s).

Response to Arguments

10. Applicant's arguments filed 05/30/07 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that Examples 1 and 2 provide the enabling disclosure for the instant invention. Applicant alleges that from the results of these examples, it can be seen that the N-acylated derivative of hydroxyproline has a preventive effect for decubitus, in addition to therapeutic treatment.

This argument is not found persuasive. The pathology of decubitus involves multitude of factors and the mechanism of decubitus ulcer formation is not yet fully known. It was generally recognized at the time of the invention was made that a good representative animal model that can quantitatively correlated to human skin is lacking (due to the substantial differences in tissue architecture and immune response between animal models and human wounds) and that further research is required in developing suitable animal model to make correlation between animal study and a practical utility in currently available form for humans, particularly the prevention of decubitus ulcers in humans (Journal of Rehabilitation Research and Development, Vol. 40, No. 1, 2003, pp. 67-72; "Animal Models for Wound Repair", Arch Dermatol Res, 1998, 290(Suppl):

S1-S11). Thus, one having ordinary skill in the art would have not predicted that the effects of reducing in skin irritation, necrosis or wound of epidermis in rabbit model study (Examples 1-2) would apply to the claimed preventive utility embraced by the instant claims.

Applicant's argument in the response takes the position that the applied reference would have neither disclosed nor would have suggested the present invention, particularly the specific dosage amounts described in claims 2 and 14 and "an acyl group having 1-24 carbon atoms" required in claims 3 and 15.

This argument is not found persuasive. Unlike the applicant's argument, Kobayashi teaches "the amount of 0.001 to 50% by weight, preferably 0.01 to 20% by weight, and most preferably 0.1 to 10%" by weight of N-acyl derivative of hydroxyproline based on the total weight which overlaps with instantly claimed "0.1 to 15% by weight to the total weight" (see para. [0009], [0016]-[0027]). Furthermore, Kobayashi teaches "an acyl group having preferably 1 to 24 carbon atoms, more preferably 1 to 12 carbon atoms and more preferably 1 to 6 carbon atoms" as the examples of the N-acyl derivatives of hydroxyproline (see para. [0016]). Thus, Kobayashi clearly anticipates the instant invention.

Applicant's argument in the response takes the position that the applied referenced would have neither disclosed nor would have suggested the presently claimed method of treatment or prevention of decutitus,

This argument is not found persuasive. The American Heritage Dictionary (Second College Edition, 1982) defines the term "prevent" as "anticipate or counter in advance, to keep

from happening". The interpretation of the instant claims allows for inclusion of treatment population where patient does not necessarily have any decubitus condition.

Thus, the prior art directing administration of the same compound(s) inherently possessing therapeutic effect, in overlapping dosage amounts, as disclosed by Applicant anticipates the Applicant's invention even absence of underlying mechanism. Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

In the instant case, the end result or intended purpose of preventing decubitus is a necessary consequence of what was deliberately intended in the prior art. Thus, Kobayashi anticipates the instant invention.

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Applicant's argument in the response takes the position that the applied referenced would have neither disclosed nor would have suggested use of the instant N-acylated derivative of hydroxyproline derivate as the active agent for the claimed utility in treating or preventing decubitus.

This argument is not found persuasive. Unlike the applicant's argument, the interpretation of the instant claims reciting open transitional language, such as "comprising", allows for the inclusion of any other unspecified ingredients even in major amounts in said

composition. Thus, Kobayashi composition comprising the claimed N-acylated derivative of hydroxyproline clearly anticipates the instant composition.

In response to the applicant's argument that USP'386 or the copending 10/250372 would have neither disclosed nor would have suggested the instant invention because the composition described in USP'386 or 10/250372 that is useful for the treatment of arthritis is not same as the instant composition that is useful for the treatment or prevention of decubitus, the examiner recognizes that the argument in the response is basically the same as discussed above, so the response discussed above applies here as well and is unpersuasive for reason just discussed.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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